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Sylvestre Marillonnet

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EXAMINER

ZHENG, LI

ART UNIT

PAPER NUMBER

1638

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/578,962	Applicant(s) MARILLONNET ET AL.	
	Examiner LI ZHENG	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 February 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-43,46-55 and 57 is/are pending in the application.
- 4a) Of the above claim(s) 1-35,39-43,46-55 and 57 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 36-38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>2/16/2010</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1-43, 46-55 and 57 are pending.

Election/Restrictions

2. Applicant's cancellations of claims 44-45, and amendments to claim 36 filed on 2/16/2010 are acknowledged.

This application contains claims 1-35, 39-43, 46-55 and 57 drawn to an invention nonelected with traverse in Paper filed 4/30/2009. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 36-38 are examined on the merits.

3. The objection to the specification is withdrawn due the amendment to the specification.
4. The rejection under U.S.C 112, Second Paragraph, is withdrawn due to claim amendment and claim cancellation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 36-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klimyuk et al. (U.S. Patent Pub. No. 2004/0255347) in view of Rose (2002, RNA 8:1444-1453) and Genbank Accession Number Z29370.

The claims are drawn to a process of transiently expressing a sequence of interest in a plant, plant part, or plant cell culture, comprising: transforming a plant, plant part, or plant cell culture with a heterologous DNA having a sequence encoding an RNA replicon operably linked or linkable to a transcription promoter, wherein said sequence encoding an RNA replicon contains (i) sequences for replicon function of said RNA replicon, said sequences being derived from a sequence of a plant RNA virus, (ii) a sequence of interest, whereby said sequences for replicon function comprise at or within A/U rich localities of said sequences for replicon function the insertion of one or more nuclear introns, whereby A/U rich localities are sequence stretches of at least 20 nucleotides in length with at least 55% A/U- content or sequence stretch of 6-9 nucleotide in a row of purely A/U containing sequence ; or wherein said transforming is performed by Agrobacterium-mediated transient transformation of T-DNA; or wherein said transforming is performed by agroinfiltrating the stem or leaves of

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tobacco plant.

Klimyuk et al. teach a process for expressing of one gene of interest from viral vector assembled from two CrTMV based provectors through site specific recombination (paragraph [0176] and claim 1; Figure 4). Klimyuk et al. teach that delivery of viral vector constructs by infiltration of agrobacterium tumefaciens suspension into Plant leaves of tobacco. Klimyuk et al. also teach the process is done by transient expressing (paragraph [0007] and claim 19). Klimyuk et al. also teach the invention allows for higher efficiency of gene expression compared to conventional system by reducing the size (paragraph [0110]). Klimyuk et al. also teach

Klimyuk et al. do not teach the limitation that one or more intron is inserted near or within A/U-rich localities of said sequence for replicon function whereby A/U rich localities are sequence stretches of at least 20 nucleotides in length with at least 55% A/U- content or sequence stretch of 6-9 nucleotide in a row of purely A/U containing sequence.

Rose teaches that insertion of heterologous intron enhance expression of gene (abstract).

Genbank Accession Number Z29370 discloses nucleotide sequence encoding a CrTMV RNA dependent RNA polymerase with numerous A/U rich localities that are sequence stretches of at least 20 nucleotides in length with at least 55% A/U- content or sequence stretch of 6-9 nucleotide in a row of purely A/U containing sequence.

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Given the recognition of those of ordinary skill in the art of the value of expressing gene of interest as taught by Klimyuk et al. , it would have been obvious for a person with ordinary skill in the art to generate an expression vector of Klimyuk et al. by inserting the intron of Rose into AT rich region of CrTMV RNA dependent RNA polymerase of Klimyuk et al in view of Genbank Accession Number Z29370, resulting in the instant invention. One skilled in the art would have been motivated to do so given the teaching of Rose that insertion of a plant intron would enhance the expression of gene of interest and the teaching of Klimyuk et al. that the expression system using viral RNA polymerase is limited by the low ability of RNA polymerase to provide function in trans (column 2, lines 18-26).. .

Thus the claimed invention would have been prima facie obvious as a whole to one of ordinary skill in the art at the time it was made, especially in the absence of evidence to the contrary.

Applicants traverse in the paper filed February 16, 2010. Applicants' arguments have been fully considered but were not found persuasive.

Applicants argue that Klimyuk et al. silent on the problem of increase the frequency with which RNA replicons appear in the cytosol, therefore a person with ordinary skill in the art has no motivation to deal with this problem (response, the paragraph bridging pages 19-20).

The Office contends that it is not required for Klimyuk et al. to deal with the same problem. As long as modified method of Klimyuk et al. contains all the

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steps as the instant invention, the instant claims are considered as being obvious over the combined prior art.

Applicants further argue that from Klimyuk et al., a person with ordinary skill in the art has no reason to consider Rose since Rose is silent on RNA viral plant expression system (response, page 20, 2nd paragraph).

The Office contends that Rose et al. do not have to teach RNA viral plant expression system. However, when a person with ordinary skill in the art look for ways to improve RNA polymerase function in trans, increasing expression of the gene is an obvious choice. Rose et al. teach one way to achieve increased expression of gene by inserting an intron into the gene.

Applicants further argue that once the transcribed replicon arrives in cytoplasm, plant viral vector replicate strongly to yield high copy number of viral RNA and given high expression levels of a protein of interest, therefore one would not expect that any sub-optimal transport into the cytoplasm could significantly affect the entire process (response, the paragraph bridging pages 20-21).

The Office contends that regardless the mechanism, inserting an intron into a gene does increase expression of the gene. As taught by Klimyuk et al., the expression system using viral RNA polymerase is limited by the low ability of RNA polymerase to provide function in trans, therefore increasing expressing of RNA polymerase by inserting an intron as taught by Rose will at least improve the expression of the gene of interest.

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Applicants further argue that claim 36 is amended such that the feature “whereby said sequences for replicon function comprise at or within A/U rich localities of said sequences for replicon function the insertion of one or more nuclear introns, whereby A/U rich localities are sequence stretches of at least 20 nucleotides in length with at least 55% A/U- content or sequence stretch of 6-9 nucleotide in a row of purely A/U containing sequence” is not taught by Klimyuk et al or Rose et al. (response, page 21, 2nd paragraph).

The Office contends that in view of Genbank Accession Number Z29370 which discloses nucleotide sequence encoding a CrTMV RNA dependent RNA polymerase with numerous A/U rich localities that are sequence stretches of at least 20 nucleotides in length with at least 55% A/U- content or sequence stretch of 6-9 nucleotide in a row of purely A/U containing sequence, CrTMV RNA dependent RNA polymerase gene of Klimyuk et al. contains those features.

Applicants final argue that it is counter intuitive for a person to consider optimization of the sequences for replicon function of DNA-encoded RNA replicon (response, page 21, 3rd paragraph).

The Office again contends that it is not counter intuitive to optimize the expression of RNA dependent RNA polymerase by inserting an intron given the teaching of Rose et al. that inserting an intron into the gene to be expressed could enhance the expression.

Conclusion

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No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Li Zheng whose telephone number is 571-272-8031. The examiner can normally be reached on Monday through Friday 9:00 AM - 5:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on 571-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Li Zheng/

Examiner, Art Unit 1638

